

*Sub C*

What we claim is:

1. An isolated polynucleotide comprising SEQ ID NO: 3.
2. An isolated polynucleotide comprising nucleotides 1-1532, 1080-1643, 1181-1643, 1292-1643, 1394-1643, or 1394-1532 of SEQ ID NO: 3.
- 5 3. The polynucleotide of claim 2, wherein the polynucleotide comprises nucleotides 1394-1532 of SEQ ID NO: 3.
4. An isolated polynucleotide that hybridizes under stringent conditions to the polynucleotide of claim 1.
- 10 5. An isolated polynucleotide that hybridizes under stringent conditions to the polynucleotide of claim 2.
6. An isolated polynucleotide comprising a nucleotide sequence that is at least 80% identical to the polynucleotide of claim 1.
7. An isolated polynucleotide comprising a nucleotide sequence that is at least 80% identical to the polynucleotide of claim 2.
- 15 8. An isolated polynucleotide that is complementary to the polynucleotide of claim 1.
9. An isolated polynucleotide that is complementary to the polynucleotide of claim 2.
10. A composition comprising the polynucleotide of claim 1 and a suitable carrier.
11. A composition comprising the polynucleotide of claim 2 and a suitable carrier.
12. A recombinant vector comprising the polynucleotide of claim 1.
13. A recombinant vector comprising the polynucleotide of claim 2.
14. A host cell comprising the recombinant vector of claim 12.
15. A host cell comprising the recombinant vector of claim 13.
- 25 16. The recombinant vector of claim 12, further comprising at least one polynucleotide encoding a heterologous polypeptide.
17. The recombinant vector of claim 13, further comprising at least one polynucleotide encoding a heterologous polypeptide.

- ●
18. The recombinant vector of claim 16, wherein said heterologous polypeptide is selected from the group consisting of luciferase,  $\beta$ -galactosidase, chloramphenicol acetyl transferase transferase, and green fluorescent protein.
19. The recombinant vector of claim 18, wherein said heterologous polypeptide is luciferase.
- 5 20. The recombinant vector of claim 19, wherein said vector is pAPR1.
21. A method suitable for increasing cholesterol efflux from cells of a mammalian subject comprising the step of administering to the mammalian subject at least one ligand for a nuclear receptor in an amount sufficient to increase cholesterol efflux from said cells.
- 10 22. The method of claim 21, wherein the ligand is selected from the group consisting of LXR, RXR, PPAR, FXR, and SXR ligands.
23. The method of claim 22, wherein said LXR ligand is selected from the group consisting of 20(S) hydroxycholesterol, 22(R) hydroxycholesterol, 24(S) hydroxycholesterol, 25-hydroxycholesterol, and 24(S), 25 epoxycholesterol.
24. The method of claim 23, wherein said ligand is 20(S) hydroxycholesterol.
25. The method of claim 22, wherein said RXR ligand is selected from the group consisting of 9-*cis* retinoic acid, retinol, retinal, all-trans retinoic acid, 13-*cis* retinoic acid, acitretin, fenretinide, etretinate, CD 495, CD564, TTNN, TTNNPB, TTAB, LGD 1069.
26. The method of claim 25, wherein said ligand is 9-*cis* retinoic acid.
27. The method of claim 22, wherein at least two ligands are administered to the mammalian subject.
28. The method of claim 27, wherein the increase in cholesterol efflux is at least 25-fold relative to the level of cholesterol efflux with either ligand alone.
29. The method of claim 27, wherein the ligands are 20(S) hydroxycholesterol and 9-*cis* retinoic acid.
- 25 30. A method suitable for increasing cholesterol efflux from cells of a mammalian subject comprising the step of administering to the mammalian subject an eicosanoid in an amount sufficient to increase cholesterol efflux in said cells.
31. The method of claim 30, wherein said eicosanoid is selected from the group consisting of prostaglandin E2, prostacyclin 12, and prostaglandin J2.

SEARCHED  
INDEXED  
SERIALIZED  
FILED

32. A method suitable for increasing the expression of ABC1 in the cells of a mammalian subject comprising the step of administering to the mammalian subject a ligand for a nuclear receptor in an amount sufficient to increase the expression of ABC1 in said cells.

33. The method of claim 32, wherein the ligand is selected from the group consisting 5 of LXR, RXR, PPAR, FXR, and SXR ligands.

34. A method for screening a test compound for ABC1 expression modulating activity comprising the steps of:

operatively linking a reporter cDNA with an expression modulating portion of the mammalian ABC1 gene to produce a recombinant reporter construct;

10 transfecting the recombinant reporter construct into a population of host cells;

assaying the level of reporter gene expression in a sample of the host cells;

contacting the host cells with the test compound being screened;

assaying the level of reporter gene expression in a sample of the host cells after contact with the test compound; and

comparing the relative change in the level of reporter gene expression caused by exposure to the test compound, thereby determining the ABC1 expression modulating activity.

35. The method of claim 34, wherein the expression modulating portion of the ABC1 gene is the 5' flanking region.

36. The method of claim 35, wherein the 5' flanking region comprises SEQ ID NO: 3.

37. The method of claim 35, wherein the 5' flanking region comprises a polynucleotide comprising nucleotides 1-1532, 1080-1643, 1181-1643, 1292-1643, 1394-1643, or 1394-1532 of SEQ ID NO: 3.

38. The method of claim 36, wherein the reporter cDNA is selected from the group consisting of luciferase,  $\beta$ -galactosidase, chloramphenicol acetyl transferase, and green 25 fluorescent protein cDNA.

39. The method of claim 34, wherein the host cell is a mammalian cell.

40. The method of claim 38, wherein the recombinant reporter construct is pAPR1.

41. A kit suitable for screening a compound to determine the ABC1 expression modulating activity of the compound comprising a recombinant reporter construct comprising a

reporter cDNA operatively linked to an expression modulating portion of the mammalian ABC1 gene in an amount sufficient for at least one assay and instructions for use.

42. The kit of claim 41, wherein the expression modulating portion of the mammalian ABC1 gene comprises the polynucleotide of claim 1.

5 43. The kit of claim 41, wherein the expression modulating portion of the mammalian ABC1 gene comprises the polynucleotide of claim 2.

44. The kit of claim 41, wherein the reporter cDNA is selected from the group consisting of luciferase,  $\beta$ -galactosidase, chloramphenicol acetyl transferase, and green fluorescent protein cDNA.

10 45. The kit of claim 42, wherein the reporter cDNA is a luciferase cDNA.

46. The kit of claim 43, wherein the reporter cDNA is a luciferase cDNA.

47. The kit of claim 45, wherein the recombinant reporter construct is pAPR1.

48. The kit of claim 41, further comprising means for detecting the reporter gene.

49. A method for identifying genes that are responsible for an inherited abnormality comprising the steps of:

a. obtaining a first RNA sample from a first individual with the abnormality;

b. obtaining a second RNA sample from a normal second individual;

c. preparing mRNA from the first RNA sample to give a first mRNA sample;

d. preparing mRNA from the second RNA sample to give a second mRNA sample;

e. preparing a labeled first cDNA sample by reverse transcribing the first mRNA sample;

f. preparing a gene expression array from the labeled first cDNA sample;

g. preparing a labeled second cDNA sample by reverse transcribing the second mRNA sample;

25 h. preparing a gene expression array from the labeled second cDNA sample; and

i. probing the first gene expression array of the labeled first cDNA sample and probing the second gene expression array of the labeled second cDNA sample and identifying the variations in gene expression between the RNA corresponding to the first cDNA sample and the RNA corresponding to the second cDNA sample.

30 50. The method of claim 49 wherein the differences between the RNA corrsponoding

to the first cDNA sample and RNA corresponding to the second cDNA sample are analyzed to identify a property selected from the group consisting of first RNA that is overexpressed in comparison to second RNA, first RNA that is underexpressed in comparison to the second RNA, first RNA that is absent in comparison to the second RNA, and first RNA that is present in comparison to second RNA.

- 5      51.     The method of claim 49 wherein the abnormality is a negative abnormality.
52.     The method of claim 49 wherein the individual is a mammal.
53.     The method of claim 52 wherein the mammal is a human.
54.     The method of claim 49 wherein at least one variation between the RNA
- 10    corresponding to the first cDNA sample and the RNA corresponding to the second cDNA sample is evaluated to determine if it contributes to the abnormality.

55.     The method of claim 49 wherein a third RNA sample is obtained from a an third individual having the same abnormality as first individual and the method of steps (a)-(g) are repeated substituting the third RNA sample for the first RNA sample and comparing the differences between the first and second and second and third to and identifying gene expression differences that are common to the abnormal individuals.

Add  
C3-